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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/117,218	01/11/1999	SUSANNE M. BROWN	117-261	3436

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EXAMINER

NGUYEN, QUANG

ART UNIT	PAPER NUMBER
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1636

24

DATE MAILED: 06/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/117,218

Applicant(s)

BROWN ET AL.

Examiner

Quang Nguyen, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 33-45 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 33-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicants' amendment filed on March 31, 2003 has been entered as Paper No. 23.

New claims 33-45 are pending in the present application.

The text of those sections of Title 35 U.S.C. Code not included in this action can be found in a prior Office Action.

### ***Claim Rejections - 35 USC § 102***

New claims 33-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Martuza et al. (U.S. Patent No. 6,139,834 with the effective filing date of June 23, 1994; Cited previously) essentially on the same ground of rejection set forth in the previous Office Action.

With respect to a method for killing tumor cells in a subject via intratumoral injection of mutant herpes simplex virus, Martuza et al. teach the delivery of a pharmaceutical composition comprising: (A) a herpes simplex virus vector that is altered in (i) the  $\gamma$ 34.5 gene, and (ii) the ribonucleotide reductase gene; and (B) a pharmaceutically acceptable vehicle for said vector, such that said tumor cells are altered *in situ* by said vector, whereby said tumor cells are killed; the same method wherein said tumor cells are selected from the group consisting of melanoma cells, pancreatic cancer cells, prostate carcinoma cells, lymphoma cells, hepatoma cells and mesothelioma and epidermoid carcinoma cells (See the entire patent and particularly claims 1 and 3). An exemplary mutant herpes simplex virus, G207, disclosed by

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Martuza et al. contains a 1-kB deletion in both copies of the  $\gamma$ 34.5 gene within the BamH1 fragment of the long terminal repeat of the viral genome (See Figures 1, 2 and column 15, lines 36-45). The mutant herpes simplex virus can be derived from either HSV-1 or HSV-2 (column 4, lines 20-22; column 7, lines 6-22; column 8, lines 5-7). The mutant herpes simplex virus can be administered to human and non-human animals suffering from tumors and neoplasms by direct intraneoplastic inoculation (column 11, lines 45-57). Moreover, the disclosed method for killing tumors and neoplasms is not necessarily limited to malignant brain tumor, such as astrocytoma, glioblastoma and others (column 11, lines 45-55; column 3, lines 61-67). Therefore, Martuza et al. clearly anticipate the instantly claimed invention.

It should be noted that the U.S. Patent No. 6,139,834 of Martuza et al. has an effective filing date of June 23, 1994 because of the support found in column 3, lines 52-58; column 12, lines 6-7; column 15, lines 41-50 and other embodiments contained in the U.S. Patent No. 5,585,096 of Martuza et al.

### ***Responses to Arguments***

Applicants' arguments related to the above rejection in the Amendment filed on March 31, 2003 in Paper No. 23 (pages 6-8) have been fully considered.

Applicants presented the following arguments: (a) The new limitation "consisting essentially of" in new claims excludes ingredients which would affect the basic and novel characteristics of the mutant herpes simplex virus defined in the claims; (b) the cited Martuza patent failed to provide an enabling disclosure of the presently claimed

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method because it does not provide specific examples of successful treatment of non-neuronal tumor cells in mammals or there is any indication of a reasonable expectation to achieve such a treatment; (c) In the Martuza patent, the cell specific promoter and the ribonucleotide reductase (RR) gene are essential features that are excluded from the scope of the present invention; and (d) the R3616 vector in the Martuza patent which is deficient in only gamma34.5 gene is not attenuated for virulence in non-neuronal cells and that incorporation of a modification to ribonucleotide reductase gene is essential for operation of selected virulence in non-neuronal tumor tumors. Applicants' arguments are respectfully found unpersuasive for the following reasons.

Firstly, with respect to the transitional phrase "consisting essentially of" in new claims, Applicants' attention is directed to *In re Herz*, 537 F.2d 549, 551-552, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original) (prior art hydraulic fluid required a dispersant which appellants argued was excluded from claims limited to a functional fluid "consisting essentially of" certain components. In finding the claims did not exclude the prior art dispersant, the court noted that appellants' specification indicated the claimed composition can contain any well-known additive such as a dispersant, and there was no evidence that the presence of a dispersant would materially affect the basic and novel characteristic of the claimed invention. The prior art composition had the same basic and novel characteristic (increased oxidation resistance) as well as additional enhanced detergent and dispersant characteristics.). In this instance, the specification teaches specifically "The HSV genome also includes a number of other genes which are non-essential to the successful culturing of the virus. Their removal

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may further contribute to the safety of the HSV mutant by further reducing neurovirulence and reducing the likelihood of recombination to the wild type.” (page 5, lines 18-23); and “Thus, in addition to the primary modification to the gamma34.5 gene of the R<sub>L</sub> region, it may be advantageous to also include in the HSV mutant one or more secondary modifications which are generally within non-essential genes unless the missing gene product can be provided in an alternative way.” (line 33 of page 5 continues to line 3 of page 6). “A consisting essentially of” claim occupies a middle ground between closed claims that are written in a consisting of format and fully open claims that are drafted in a comprising.” Format. For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, “consisting essentially of” will be construed as equivalent to “comprising.” See, e.g., *PPG, 156 F.3d* at 1355, 48 USPQ2d at 1355 (“PPG could have defined the scope of the phrase consisting essentially of” for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention.”). See also *In re Janakirama-Rao*, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of “consisting essentially of,” applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristic of applicant’s invention. Accordingly, the instant claims still read over the teachings of Martuza et al.

Secondly, it should also be noted that claims of an issued U.S. Patent is presumed to be valid and that the enabled scope of an issued U.S. Patent is not limited by the exemplification.

Thirdly, there is nowhere in the Martuza's patent indicating or suggesting that the modification of the ribonucleotide reductase gene or the utilization of cell specific promoter as essential features for killing any tumor cells, including non-neuronal tumor cell, which is the main feature of the presently claimed invention. The passage in col. 6, lines 40-45, in the Martuza's patent indicates the herpes simplex virus RR-mutants are attenuated for neurovirulence and less likely to propagate in the event of a fever in the infected host, and that these characteristics are essential to a therapeutic vector which must be of attenuated neurovirulence and amenable to antiviral therapy in the event of viral encephalitis. The herpes simplex virus mutant deficient in only the gamma34.5 gene such as R3616 is neuronal avirulent due to latency of gamma34.5 mutants, but it possesses an ability to result in sustained protein synthesis and production of infectious progeny in non-neuronal cells (see Roizman et al., U.S. Patent No. 6,340,673), and even more so in non-neuronal cancer cells that result ultimately to the lysis of non-neuronal cancer cells.

Accordingly, new claims 33-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Martuza et al. for the reasons set forth above.

New claims 33-34, 37-39 and 41-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Roizman et al. (U.S. Patent No. 6,340,673) essentially on the same ground of rejection already set forth in the previous Office Action.

Roizman et al. teach using an HSV-1 virus with a specific mutation in the gamma 35.4 gene to treat cancer and tumorigenic diseases both in the CNS and in all other parts of the body in a mammal including human, not necessarily limited to tumors of the CNS (see col. 5, lines 63-66; col. 9, lines 50-61; and the claims). Roizman et al. further teach direct injection of the virus into the tumor or intratumorally, and that an exemplified HSV-1 virus with a specific mutation in the gamma 35.4 gene is the recombinant virus R3617 or R3616 lacking 1kb of DNA in each copy of the gamma 34.5 gene (see Table 1 of col. 17; Fig. 2). Roizman et al. also teach that infection of cells of neuronal origin with mutants incapable of expressing the gamma 34.5 gene resulted in shutoff of cellular protein synthesis, whereas infection of cells of non-neuronal origin with wild type or mutant viruses resulted in sustained protein synthesis and production of infectious progeny (col. 18, lines 10-15).

Accordingly, the teachings of Roizman et al. meet every limitation of the instant claims, and therefore the reference anticipates the instant claimed invention.



***Responses to Arguments***

Applicants' arguments related to the above rejection in the Amendment filed on March 31, 2003 in Paper No. 23 (pages 8-10) have been fully considered.

Applicants argue basically that Roizman as a whole provides no specific teaching of treatment of non-neuronal cancer with the herpes simplex virus mutants, particularly the lack of specific examples for the use of herpes simplex virus mutants in treatment of non-neuronal tumors. Applicants further argue that Roizman emphasizes the lack of attenuated virulence of mutant herpes simplex virus in non-neuronal cells, and therefore non-neuronal tumor specific cell killing is not perceived as being achievable using the teaching of Roizman.

Applicants' arguments are respectfully found to be unpersuasive because claims of an issued U.S. Patent is presumed to be valid and that the enabled scope of an issued U.S. Patent is not limited by the exemplification. Claims of the patent issued to Roizman clearly indicate that a herpes simplex virus vector lacking an expressible gamma 34.5 gene can be used to suppress any tumor growth, not necessarily limited to neuronal tumor growth.

***Claim Rejections - 35 USC § 103***

New claims 33-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martuza et al. (U.S. Patent No. 6,139,834 with the effective filing date of June 23, 1994; Cited previously) in view of either MacLean et al. (J. Gen. Virol. 72:631-639, 1991, Cited previously) or Brown et al. (WO 92/13943 with a publication date of August

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20, 1992; PTO-1449, IDS) and Markert et al. (Neurosurgery 32:597-603, 1993; IDS) essentially on the same ground of rejection as set forth in the previous Office Action.

With respect to a method for killing tumor cells in a subject via intratumoral injection of mutant herpes simplex virus, Martuza et al. teach the delivery of a pharmaceutical composition comprising: (A) a herpes simplex virus vector that is altered in (i) the  $\gamma 34.5$  gene, and (ii) the ribonucleotide reductase gene; and (B) a pharmaceutically acceptable vehicle for said vector, such that said tumor cells are altered *in situ* by said vector, whereby said tumor cells are killed; the same method wherein said tumor cells are selected from the group consisting of melanoma cells, pancreatic cancer cells, prostate carcinoma cells, lymphoma cells, hepatoma cells and mesothelioma and epidermoid carcinoma cells (See the entire patent and particularly claims 1 and 3). An exemplary mutant herpes simplex virus, G207, disclosed by Martuza et al. contains a 1-kB deletion in both copies of the  $\gamma 34.5$  gene within the BamH1 fragment of the long terminal repeat of the viral genome (See Figures 1, 2 and column 15, lines 36-45). The mutant herpes simplex virus can be derived from either HSV-1 or HSV-2 (column 4, lines 20-22; column 7, lines 6-22; column 8, lines 5-7). The mutant herpes simplex virus can be administered to human and non-human animals suffering from tumors and neoplasms by direct intraneoplastic inoculation (column 11, lines 45-57). Moreover, the disclosed method for killing tumors and neoplasms is not necessarily limited to malignant brain tumor, such as astrocytoma, glioblastoma and others (column 11, lines 45-55; column 3, lines 61-67).

Martuza et al. do not teach a method of killing tumor cells in a subject using the mutant herpes simplex virus wherein there is a deletion from 0.7 to 0.8 kb of the BamH1 restriction fragment of the long terminal repeat of the viral genome, or wherein the mutant herpes simplex virus is strain 1716.

Both MacLean et al. and Brown et al. disclose HSV-1 mutant 1716 and they both teach that strain 1716 contains a 759 bp deletion in the  $\gamma$ 34.5 gene which is found within the BamH1 s fragment of the long repeat region of the viral genome (See abstract and Fig. 3 on page 634 of MacLean et al.; page 4, lines 16-31 in Brown et al.). The deletion is associated with the non-neurovirulence for strain 1716 comparing to the parental wild type strain.

Markert et al. teach a herpes simplex virus-1 called R3616 with decreased neurovirulence (See abstract) and the virus contains a 1kb deletion in the  $\gamma$ 34.5 gene (page 598, column 1, bottom of third paragraph). Markert et al. further teach that R3616 possesses antineoplastic effects and it significantly prolonged average survival without producing premature encephalitic deaths in a nude mouse intracranial glioma model (See abstract).

Accordingly, it would have been obvious to one of ordinary skilled in the art at the time of invention was made to substitute any of the mutant herpes simplex virus utilized in the method disclosed by Martuza et al. with the mutant virus strain 1716 taught by MacLean et al. or Brown et al., and one of ordinary skilled in the art would have a reasonable expectation of success for killing tumor cells in a subject via an intratumoral route of delivery. This is because it was well known in the art that mutant herpes

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simplex virus having a deletion in the  $\gamma$ 34.5 gene has reduced non-neurovirulence and still possesses anti-neoplastic effects as exemplified by the teachings of Markert et al. and Martuza et al. Additionally, one of ordinary skilled artisan would have been motivated to carry out the above modification because the mutant virus strain 1716 has been known in the art to be non-neurovirulent comparing to the parental wild type strain, and therefore the brain of treated mammals is protective from its utilization.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

### ***Responses to Arguments***

Applicants' arguments related to the above rejection in the Amendment filed on March 31, 2003 in Paper No. 23 (pages 10-12) have been fully considered.

Applicants argue basically that Martuza teaches modification of ribonucleotide reductase as being essential, and therefore the ordinary skilled person was directed to consider such modification to ribonucleotide reductase being essential to any further modifications of Martuza such that the ordinarily skilled person was led away from the presently claimed invention.

Applicants' arguments are respectfully found to be unpersuasive for the same reasons already set forth in the Response to the Arguments related to the rejection of claims 33-43 above.

New claims 33-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roizman et al. (U.S. Patent No. 6,340,673) in view of Martuza et al. (U.S. Patent No. 6,139,834) and either MacLean et al. or Brown et al. essentially on the same ground of rejection already set forth in the previous Office Action.

Roizman et al. teach using an HSV-1 virus with a specific mutation in the gamma 35.4 gene to treat cancer and tumorigenic diseases both in the CNS and in all other parts of the body in a mammal including human, not necessarily limited to tumors of the CNS (see col. 5, lines 63-66; col. 9, lines 50-61; and the claims). Roizman et al. further teach direct injection of the virus into the tumor or intratumorally, and that an exemplified HSV-1 virus with a specific mutation in the gamma 35.4 gene is the recombinant virus R3617 or R3616 lacking 1kb of DNA in each copy of the gamma 34.5 gene (see Table 1 of col. 17; Fig. 2). Roizman et al. also teach that infection of cells of neuronal origin with mutants incapable of expressing the gamma 34.5 gene resulted in shutoff of cellular protein synthesis, whereas infection of cells of non-neuronal origin with wild type or mutant viruses resulted in sustained protein synthesis and production of infectious progeny (col. 18, lines 10-15).

Roizman et al. do not specifically teach a method for treating mesothelioma, ovarian carcinoma, bladder cancer or melanoma using the recombinant virus R3617 or R3616. Nor do Roizman et al. specifically teach the use of the mutant herpes simplex virus in which the deletion in the gamma 35.4 gene is from 0.7 to 0.8 kb or the use of the mutant herpes simplex virus strain 1716.

However, at the effective filing date of the present application, Martuza et al. already teach the delivery of a pharmaceutical composition comprising: (A) a herpes simplex virus vector that is altered in (i) the  $\gamma$ 34.5 gene, and (ii) the ribonucleotide reductase gene; and (B) a pharmaceutically acceptable vehicle for said vector, such that said tumor cells are altered *in situ* by said vector, whereby said tumor cells are killed; the same method wherein said tumor cells are selected from the group consisting of melanoma cells, pancreatic cancer cells, prostate carcinoma cells, lymphoma cells, hepatoma cells and mesothelioma and epidermoid carcinoma cells (See the entire patent and particularly claims 1 and 3). An exemplary mutant herpes simplex virus, G207, disclosed by Martuza et al. contains a 1-kB deletion in both copies of the  $\gamma$ 34.5 gene within the BamH1 fragment of the long terminal repeat of the viral genome (See Figures 1, 2 and column 15, lines 36-45). Additionally, at the effective filing date of the present application, both MacLean et al. and Brown et al. disclose HSV-1 mutant 1716 and they both teach that strain 1716 contains a 759 bp deletion in the  $\gamma$ 34.5 gene which is found within the BamH1 s fragment of the long repeat region of the viral genome (See abstract and Fig. 3 on page 634 of MacLean et al.; page 4, lines 16-31 in Brown et al.). The deletion is associated with the non-neurovirulence for strain 1716 comparing to the parental wild type strain.

Accordingly, it would have been obvious to one of ordinary skilled in the art at the time of invention was made to use the recombinant virus R3617 or R3616 lacking 1kb of DNA in each copy of the gamma 34.5 gene of Roizman et al. to lyse or kill mesothoma, ovarian, bladder or melanoma cells in light of the teachings of Martuza et al. One of

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ordinary skilled artisan would have been motivated to do so because Martuza et al. already teach that the mutant herpes simplex virus comprising a 1-kB deletion in both copies of the  $\gamma 34.5$  gene is capable of killing mesothelioma, ovarian, bladder or melanoma cells. It is further noted that the mutant herpes simplex virus taught by Maruza et al. further contains an alteration in the ribonucleotide reductase gene, which is not essential to the killing of non-neuronal cancer cells, but mainly for the purpose of reducing the possibility of the mutant herpes simplex virus to revert to the wild-type virus (col. 5, lines 40-42).

Similarly, it would also have been obvious and within the scope of skill for an ordinary skilled artisan to substitute the mutant herpes simplex virus utilized in the method disclosed by Roizman et al. with the mutant virus strain 1716 taught by either MacLean et al. or Brown et al. One of ordinary skilled in the art would have been motivated to carry out the modification and expected to successfully killing tumor cells in a subject via an intratumoral route of delivery using the mutant virus strain 1716 because it was already known in the art that a mutant herpes simplex virus having a deletion in the  $\gamma 34.5$  gene has reduced non-neurovirulence and still possesses anti-neoplastic effects as exemplified by the teachings of Roizman et al. and Martuza et al., particularly the mutant virus strain 1716 has been known in the art to be non-neurovirulent comparing to the parental wild type strain, and therefore the brain of treated mammals is protective from its utilization.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

### ***Responses to Arguments***

Applicants' arguments related to the above rejection in the Amendment filed on March 31, 2003 in Paper No. 23 (pages 10-12) have been fully considered.

Applicants argue basically that Roizman teaches no expectation of success in treatment of non-neuronal cancer, and that Roizman directed the ordinary skilled person to the conclusion that a non-neuronal cell avirulence phenotype necessary for inducement of tumour cell specific kill in non-neuronal cancer is not characteristic of herpes simplex virus mutants containing non-functional gamma 34.5 genes.

Applicants' arguments are respectfully found to be unpersuasive because claims of an issued U.S. Patent is presumed to be valid and that the enabled scope of an issued U.S. Patent is not limited by the exemplification. Claims of the patent issued to Roizman clearly indicate that a herpes simplex virus vector lacking an expressible gamma 34.5 gene can be used to suppress any tumor growth, not necessarily limited to neuronal tumor growth.

### ***Conclusions***

***No claims are allowed.***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).



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A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (703) 308-1906, or SPE, Irem Yucel, Ph.D., at (703) 305-1998.

**To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636.**

*Quang Nguyen, Ph.D.*

  
DAVID GUZO  
PRIMARY EXAMINER